



DELVE

DEEs & LGS—Voices of Experience

PATIENT FOCUSED DRUG DEVELOPMENT MEETING

Developmental and Epileptic Encephalopathies | Lennox-Gastaut Syndrome

November 1, 2019

9:00 a.m. – 12:30 p.m.

College Park Marriott Hotel &
Conference Center
Hyattsville, Maryland

ORGANIZED & HOSTED BY:

LGS FOUNDATION
LENNOX-GASTAUT SYNDROME



#LennoxGastaut

#Epilepsy

#RareDisease

#PFDD



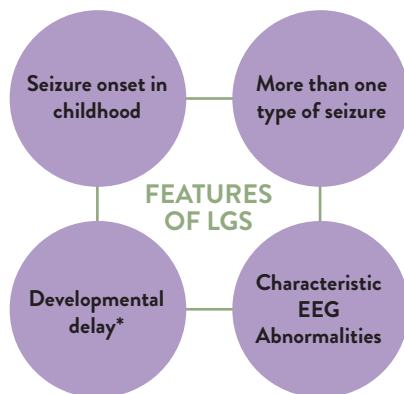
TODAY'S FOCUS

Developmental and Epileptic Encephalopathies (DEEs)

DEEs are the most severe group of epilepsies, typically beginning in early life. They are characterized by frequent uncontrolled seizures, often of multiple types, and developmental delay or intellectual disability. A key concept underpinning the term “epileptic encephalopathy” (EE) is the presence of frequent epileptiform activity that itself contributes to developmental slowing or regression. The term was recently expanded to include “developmental” in recognition that many of the underlying etiologies of the DEEs result in developmental impairment in their own right, with the superimposed EE process further adversely impacting an individual’s development. DEEs can be categorized into epilepsy syndromes, such as West Syndrome and Lennox-Gastaut Syndrome (LGS) based on characteristic symptoms and specific abnormal brain wave patterns seen on EEG. Understanding of the etiologies of the DEEs has exploded in recent years allowing further categorization of the DEEs and a causative pathogenic genetic or genomic variant is seen in around 50 percent of patients, with most arising de novo. The incidence of DEEs overall is estimated as 0.27/1000 to 0.54/1000 per year and are associated with a lifetime of severe disability and premature mortality.

Lennox-Gastaut Syndrome (LGS)

LGS is a severe Developmental and Epileptic Encephalopathy (DEE) characterized by multiple seizure types, specific EEG features, and cognitive impairment. The onset of LGS is usually between 1-8 years of age with a peak of 3-5 years of age. LGS can arise secondary to a number of underlying etiologies, including early life brain injuries (33%), congenital brain malformations (17%), infection (15%), genetic defects (15%), and metabolic disorders (9%). There are an estimated 40,000-60,000 LGS patients in the U.S. and more than 80 percent continue to have seizures, while greater than 90 percent are living with multiple chronic conditions, including severe intellectual and physical disabilities. There is a 14-fold increased risk for mortality in LGS (up to 15% of patients), but patients may live into their 40s and 50s, making caring for those with LGS is a lifelong process.



Developmental delay is not required to make the LGS diagnosis and 30% of kids are typically developing at diagnosis.

Patient-Focused Drug Development & the DELVE Meeting

In 2013, the U.S. Food and Drug Administration (FDA) began holding a series of meetings to hear directly from patients, caregivers, advocates, and other key community stakeholders about what it’s like to live with various medical conditions and how well available treatments are meeting patients’ needs. This meeting series, called the “Patient-Focused Drug Development” initiative or PFDD, has now been expanded to enable patient organizations to host PFDD meetings in collaboration with FDA. (See <http://bit.ly/FDA-PFDDinfo>)

The Lennox-Gastaut Syndrome (LGS) Foundation was approved to hold a meeting on the Developmental and Epileptic Encephalopathies (DEEs), including LGS, and is hosting the DELVE: DEEs & LGS – Voices of Experience Initiative.

The purpose of PFDD meetings in general and the DELVE meeting is for FDA staff, researchers, and developers of drugs and medical devices to understand more fully the burdens of living with a particular medical condition, as well as what patients most value in terms of treatment benefits and the risks and side effects they are willing to tolerate. An example of how PFDD can benefit people living with DEEs, including LGS, is to deepen understanding about all the ways in which DEEs impact people’s lives – including and beyond the horrific seizures, which are often the primary focus. Your active participation during this meeting will help depict the full range of experiences with DEEs and will allow these key audiences to DELVE into the Voices of DEE experience.

Learn more about the LGS Foundation on page 8 of this program.

TODAY'S AGENDA

- 8:30 – 9:00 am** **Registration**
- 9:00 – 9:05 am** **Welcome**
Christina SanInocencio, *Executive Director, LGS Foundation*
- 9:05 – 9:10 am** **About this Meeting: Developmental and Epileptic Encephalopathies (DEEs) and Lennox-Gastaut Syndrome (LGS)**
Tracy Dixon-Salazar, PhD, *Director of Research and Strategy, LGS Foundation*
- 9:10 – 9:20 am** **Patient-Focused Drug Development at the U.S. Food & Drug Administration (FDA)**
Michelle Campbell, PhD, *Center for Drug Evaluation and Research, FDA*
- 9:20 – 9:40 am** **Overview of Diagnosis and Management of DEEs and LGS**
Kelly Knupp, MD, MSCS, FAES, *University of Colorado, Denver*
- 9:40 – 9:45 am** **Introduction of Meeting Session Format**
Kim McCleary, *Moderator*
- 9:45 – 11:05 am** **Topic 1: Disease Symptoms and Daily Impacts of DEEs and LGS**
- Key Questions:**
- What was the early period of the condition like, as symptoms emerged and medical consultation/diagnosis was sought?
 - Of all the symptoms experienced because of condition, which 1 to 3 symptoms have the **most significant impact** on your child's life?
 - What are the greatest impacts on daily living and function? How have abilities and impairments evolved over time?
- Panel Remarks**
Moderated Discussion Among Meeting Participants with Lived Experience
- 11:05 – 12:25 pm** **Topic 2: Current and Future Approaches to Treatment**
- Key Questions:**
- What therapies are being used to help treat the condition or its symptoms?
 - How well is the current therapy regimen working?
 - What are the most significant downsides to current treatments being used and how do these downsides affect daily life?
 - How has treatment regimen changed over time? What contributed/led to changes?
 - Which 1-2 aspects of the condition are most important to relieve/control/reverse?
 - What has your experience been with regard to clinical trials?
 - Assuming there is no complete cure, what specific things would you look for in an ideal therapy?
- Panel Remarks**
Moderated Discussion Among Meeting Participants with Lived Experience
- 12:25 – 12:30 pm** **Closing Remarks**
Kim McCleary
- 12:30 pm** **Lunch**
Network with participants for the afternoon PFDD meeting on CDKL-5 Deficiency Disorder

ACKNOWLEDGEMENTS

With gratitude for the following individuals who have enhanced the **DELVE** PFDD Meeting:

Meghana Chalasani of the FDA's Office of Strategic Initiatives, Center for Drug Evaluation and Research for providing counsel and encouragement throughout the entire planning process.

Kim McCleary of the Kith Collective for support with strategic, communications, and moderation of today's meeting.

Julie Rathjens of Hello Brand for design of the DELVE logo and production of other creative materials, including this program booklet.

Our many non-profit organization friends and collaborators in the **Rare and Catastrophic Seizures Collaborative (RCSC)** who serve patients and families living with DEEs.

Families who participated in the 2018 "LGS Characteristics and Major Concerns Survey," summarized on pages 6-7 of this program.

OUR PANELISTS

The purpose of today's meeting is to better understand the experience of children, teens, and adults living with DEEs, including LGS. Panelists have dedicated additional time to speak to the challenges, expectations, and hopes of the community as a way of inviting an even broader range of experiences through the moderated discussion. We deeply appreciate their courage and dedication to the success of this meeting.

Andee Cooper, speaking on behalf of her son, Kannon (Tulsa, Oklahoma)

Tracy Dixon-Salazar, speaking on behalf of her daughter, Savannah (San Diego, California)

Jennifer Griffin, speaking on behalf of her son, Theo (Santa Barbara, California)

Karen Groff, speaking on behalf of her son, Dan (Upper Arlington, Ohio)

Kathy Leavens, speaking on behalf of her son, Matthew (Spring Hill, Florida)

Nicole Salazar, speaking on behalf of her son, Jeremiah (San Bernardino CA)

Christina SanInnocencio, speaking about her brother, Michael (Sayville, New York)

Elizabeth Terry, speaking on behalf of her daughter, Spencer (St. Louis, Missouri)

Dale Todd, speaking on behalf of his son, Adam (Cedar Rapids, Iowa)

INVITED SPEAKERS



Dr. Michelle Campbell is the Senior Clinical Analyst for Stakeholder Engagement and Clinical Outcomes for the Division of Neurology Products in the FDA's Center for Drug Evaluation and Research. Dr. Campbell's focus is in patient-focused drug development and the use of patient experience data in the regulatory setting. Prior to joining FDA, Dr. Campbell spent more than 10 years conducting research in the academic-clinical setting, including five years in a neurology and developmental medicine department. Dr. Campbell earned her BA in Biology from the College of Notre Dame, her MS in Health Science (concentration in Community Health Education) from Towson University and her PhD in Pharmaceutical Health Services Research from the University of Maryland School of Pharmacy.



Dr. Kelly Knupp is an Associate Professor of Pediatrics and Neurology at the University of Colorado. She received her medical degree from the University of New Mexico - School of Medicine, completed her residency in Pediatrics at Children's Hospital of NY followed by a Pediatric Neurology Residency at Columbia University at Children's Hospital of NY. She trained as a Clinical Fellow in Pediatric Epilepsy at the Columbia Comprehensive Epilepsy Center at NY Presbyterian Hospital. Dr. Knupp now practices at Children's Hospital Colorado in Aurora, where she is the Associate Research Director of the Neuroscience Institute and Director of the Dravet Program. Her interests are epileptic encephalopathies including Dravet Syndrome and infantile spasms.

CORPORATE SPONSORS

Thank you to these generous sponsors for their support of the DELVE meeting:



ZOGENIX

LGS CHARACTERISTICS AND MAJOR CONCERNS SURVEY

In 2018, the LGS Foundation conducted an in-depth survey of its 4,500 member patient and family community to better understand the frequency of symptoms seen in LGS, aspects of seizure treatment, and patient priorities. The survey was designed, with permission, from a survey of a similar Developmental and Epileptic Encephalopathy (DEE, Villas et al., 2017). 56 questions were asked in varying formats and it took an average of 20 minutes to complete.

Demographics

A total of 413 individuals from 17 counties (89% U.S.) responded to the survey. Only one respondent had LGS. The remaining were family members answering on behalf of a loved one. Ages for the individual with LGS ranged from 7 months to 60 years.

(N=413)

RESPONDENTS

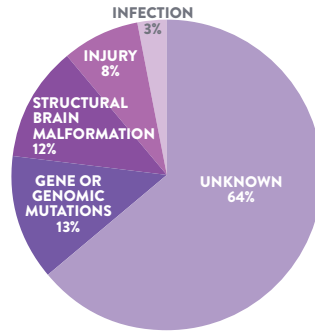
Individual with LGS	0.2%
Caregivers/family members	99.8%

INDIVIDUALS WITH LGS

Female	41%
Male	59%
Current age (3 years or younger)	4%
Current age (4-15 years)	49%
Current age (16-25 years)	29%
Current age (26-60 years)	18%

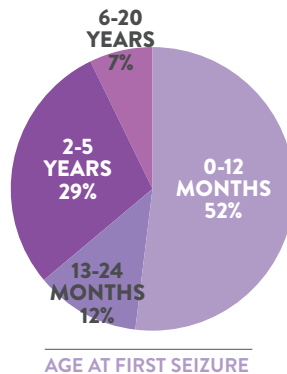
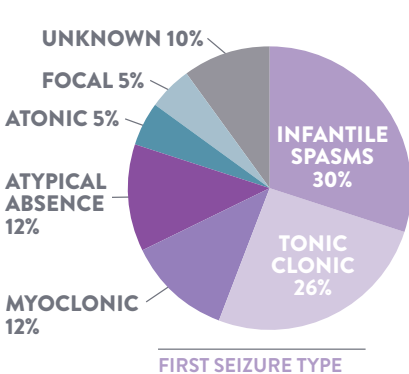
Cause/Etiology

A diverse number of causes of the seizures were reported. The majority (64%) did not know the cause. For genomic causes, 41 different genes/gene regions were reported. 94% of respondents said an EEG showing slow-spike and wave was present at some point in the disease.



Seizure Onset

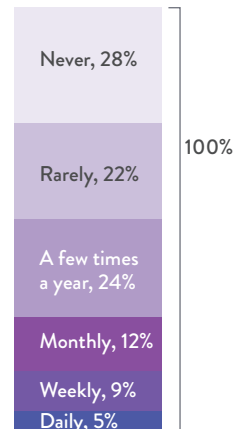
45% reported previous infantile spasms even if it was not the first seizure type. 72% said it took more than 1 year to get a diagnosis of LGS (range 1-20 years).



Seizure Injuries

81% report ever having a seizure-related head injury. Frequency of injuries in the last 12 months are listed below.

HEAD INJURIES IN THE LAST 12 MONTHS



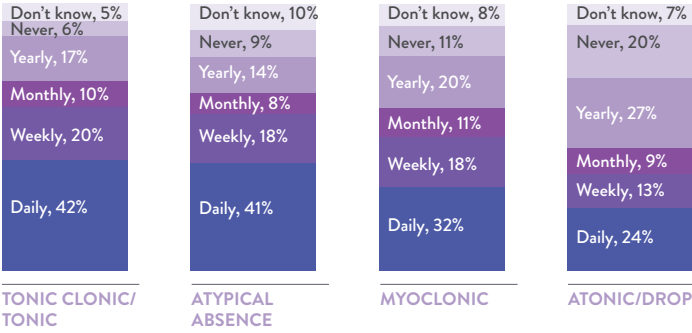
LGS and the many DEEs it is associated with represent a lifelong disability for most patients. Patients experience seizures throughout their lifetime, frequent injuries and hospitalizations, and many comorbid conditions. This survey highlights major unmet needs for better treatments for LGS and offers insight into caregiver priorities on the backdrop of the multiple chronic conditions seen in LGS. This work identifies potential areas where therapies and supportive services would be meaningful.

LGS CHARACTERISTICS AND MAJOR CONCERNS SURVEY

Current Seizure Frequency

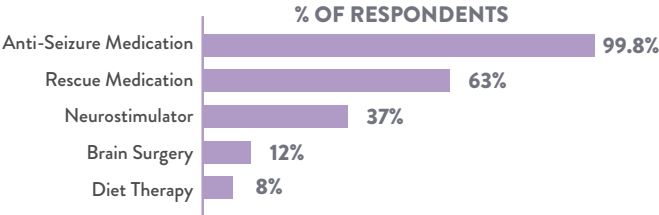
55% of respondents said the person with LGS was currently having 4 or more types of seizures. 42% said the person with LGS was having 1-3 types of seizures. Only 3% reported seizure freedom. The most problematic seizure types currently present were 1) Tonic Clonic, 2) Tonic, 3) Atonic, 4) Myoclonic, 5) Atypical Absence.

TYPE AND FREQUENCY OF CURRENT, MOST PROBLEMATIC SEIZURES



Current Treatments

Treatments for LGS include medications, neurostimulation, brain surgery, diets, and alternative therapies. Respondents report that on average they have tried 10-12 seizure drugs to date. The frequency of those currently on a given treatment are reported below.



Current Number of Anti-Seizure Drugs Used

- 99.8% currently use anti-seizure drugs
- 75% report the person with LGS is taking 3 or more drugs (range 3-10)
- 25% report the person with LGS is taking 1 or 2 drugs
- One respondent reported zero medication use
- The top 5 medications reported were Clobazam, Valproate, Rufinamide, Levetiracetam, and Cannabidiol.

Most common respondent concerns in the open response section:

1. Seizures & safety
2. Developmental delay, especially communication
3. Behaviors, especially aggression
4. Mobility & physical care issues
5. Sleep disturbances
6. Medical costs & access to care
7. Social isolation

Seizure Clusters and Status Epilepticus

- 94% have experienced seizure clusters
- 65% have had seizures lasting longer than 5 minutes
- 63% report using at home rescue medicines in the last 12 months

Symptoms Other than Seizures

LGS has far reaching effects beyond just seizures. Issues with development, communication, psychiatric symptoms, sleep, behavior, and mobility are common. The frequency of the most commonly reported issues in these domains are shown below.

ISSUE	%
DEVELOPMENTAL	
Severe Development Delay	80%
Moderate Delay	18%
Mild Delay	2%
COMMUNICATION	
Unable to read	72%
Unable to write	69%
Non-verbal	60%
PSYCHIATRIC	
Aggression	59%
Irritability/Agitation	41%
Impulsiveness	33%
SLEEP	
Sleep Disturbances	87%
Nocturnal Seizures	81%
Insomnia	58%
AUTISTIC FEATURES	
Diagnosed with Autism	26%
Repetitive body movements	39%
Tactile sensitivity or sensory issues	38%
MOBILITY	
Uses a wheelchair or adaptive stroller	73%
FEEDING	
Tube fed	27%

LGS FOUNDATION

LENNOX-GASTAUT SYNDROME



Our Mission:

The LGS Foundation is a nonprofit organization dedicated to improving the lives of individuals affected by LGS through research, family, support programs, and education.

Our Vision:

A world without LGS.

Our Core Values & Guiding Principles:

Families First: We work for those living with LGS. This means we ask questions and listen to LGS families as we represent their voices.

Community: We're all in this together. We seek to build a community of support and collaboration that will have a real impact. We value efficiency, community benefit, upward progress, partnering, continual learning, data-driven practices, transparency, and mutual respect.

Tirelessness: We will never give up.



Our Programs & Activities

Support & Empower Families

- Patient Assistance Program
- Patient & Family Scholarships
- Give Kids the World Partnership
- LGS Ambassadors Program
- Online LGS Support Groups
- Local LGS Meet-ups
- Community Needs Assessment Activities

Accelerate Research

- LGSF Research Grants
- LGS Exome Project
- Rare Epilepsy Network
- Professional Advisory Board
- National Presence Activities (AES, Symposia)
- Sponsorships & Travel Awards
- Community Priorities Survey Activities
- Clinical Trials Activities
- LGS Researcher Meetings

Education and Community Building

- International LGS Awareness Day
- Professional and Family Conferences (US, UK)
- Annual LGS Walk n' Wheel
- Team LGSF at the Annual Epilepsy Walk
- Educational Materials and Educational Forums
- Annual Appeal

STAY IN TOUCH:

Web: LGSFoundation.org

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Phone: 718-374-3800

Facebook: [Facebook.com/lgsfoundation](https://www.facebook.com/lgsfoundation)

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